

### **Abstract**

The present invention relates to dihydrofolate reductase inhibitors having an aromatic group and a heteroaromatic group linked by a methylene group; methods of preparation of dihydrofolate reductase inhibitors that include metal mediated cross coupling of an aromatic halide or heteroaromatic halide with an organozinc reagent; and methods of treatment and pharmaceutical compositions that utilize or comprise one or more of such dihydrofolate reductase inhibitors.